```
FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 17:04:18 ON 01 JUN 2004
L1             3 S "HYPERMUTABLE BACTERIA"
L2             1 DUP REM L1 (2 DUPLICATES REMOVED)
L3         29934 S MISMATCH
L4        272879 S REPAIR
L5         10297 S L3 (S) L4
L6           547 S PMS2 OR PMSR OR PMS2L
L7           397 S L5 (P) L6
L8           208 S L7 NOT PY>=2001
L9            90 DUP REM L8 (118 DUPLICATES REMOVED)
L10           16 S L8 AND BACTER?
L11            4 S L9 AND BACTERIA
L12      2343761 S PROKARYOTE OR BACTER?
L13            7 S L9 AND L12
L14            7 DUP REM L13 (0 DUPLICATES REMOVED)
L15            0 S HYPERMUTAB LE
L16          627 S HYPERMUTABLE
L17          131 S L16 AND L12
L18           71 DUP REM L17 (60 DUPLICATES REMOVED)
L19           44 S L18 NOT PY>=2001
L20           48 S L18 NOT PY>=2002
L21           14 S L20 AND MISMATCH
L22            0 S L20 AND L6
L23            9 S L16 AND L6
L24            3 DUP REM L23 (6 DUPLICATES REMOVED)
```

ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002299004 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12039884
TITLE: Response of Escherichia coli hypermutators to selection pressure with antimicrobial agents from different classes.
AUTHOR: Miller Keith; O'Neill Alexander John; Chopra Ian
CORPORATE SOURCE: Antimicrobial Research Centre and Division of Microbiology, School of Biochemistry and Molecular Biology, University of Leeds, Leeds LS2 9JT, UK.
SOURCE: Journal of antimicrobial chemotherapy, (2002 Jun) 49 (6) 925-34.
Journal code: 7513617. ISSN: 0305-7453.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020602
Last Updated on STN: 20030111
Entered Medline: 20030110

AB The responses of hypermutable Escherichia coli strains to selection with antibiotics having different endogenous resistance potentials were determined. Selections with rifampicin or ciprofloxacin at 4 x MIC, i.e. conditions where they act as single target agents against RpoB and GyrA, respectively, demonstrated that some hypermutators generated resistant mutants with frequencies up to 1000-fold higher than normal strains. Furthermore, individual mutants recovered from hypermutable hosts often exhibited higher levels of resistance to the drugs than mutants arising in normal hosts. Exposure to ciprofloxacin at 16 x MIC, i.e. conditions where it has low endogenous resistance potential, failed to select resistant mutants in hypermutable or normal hosts (mutation frequency <10(-11)). Consistent with these findings, the highest estimated mutation frequency for selection at 16 x MIC in a hypermutable host would be 4.4 x 10(-15) (mutT), calculated by determining the individual mutation frequencies for first-step ciprofloxacin resistance and second-step resistance arising in hosts already harbouring single first-step mutations in gyrA at codons 83 or 87. The frequency with which second-step ciprofloxacin resistance mutations arose was suppressed in hypermutators and demonstrated at most a 10-fold increase in mutation rate compared with non-hypermutator hosts. Second-step mutants may contain mutations in mar, since a survey of 170 second-step ciprofloxacin-resistant mutants derived from both hypermutator and non-hypermutator parents demonstrated that they all possessed increased resistance to chloramphenicol, a phenotype associated with mar mutations. Exposure to 4 x MIC of D-cycloserine, cefotaxime or polymyxin B (agents with multiple targets or membrane activity) failed to select resistant mutants in normal or hypermutator hosts (mutation frequency <10(-11)); however, continuous culture in the presence of sub-lethal concentrations of D-cycloserine (0.25 x MIC) selected resistant mutants in hypermutators after c. 33 generations, compared with c. 44 generations in normal hosts. Since **hypermutable bacteria** occur naturally, our data emphasize that successful new drugs will need to possess low endogenous resistance potentials.

ANSWER 1 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2000296662 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10837019
TITLE: Tumors arising in DNA mismatch repair-deficient mice show a wide variation in mutation frequency as assessed by a transgenic reporter gene.
AUTHOR: Baross-Francis A; Milhausen M K; Andrew S E; Jevon G; Jirik F R
CORPORATE SOURCE: Centre for Molecular Medicine and Therapeutics, Department of Medicine, University of British Columbia, Vancouver, BC V5Z 4H4, Canada.
SOURCE: Carcinogenesis, (2000 Jun) 21 (6) 1259-62.
Journal code: 8008055. ISSN: 0143-3334.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000803

AB We reported previously that thymic lymphomas arising in mice lacking the DNA **mismatch repair** (MMR) gene, Msh2(-/-), exhibited striking elevations in the mutation frequency of a transgenic lacI reporter gene when compared with normal Msh2(-/-) tissues. To investigate whether hypermutation was a feature of all tumors arising in MMR-deficient mice, lacI transgene mutation frequencies were obtained from several different mouse tumors deficient for **PMS2** and/or MSH2. While lacI gene hypermutation was again clearly evident in Msh2 +/- ms2(-/-) and Msh2(-/-)**Pms2**(-/-) thymic lymphomas, three non-thymic MSH2-deficient tumors failed to show lacI gene mutation frequency elevations when compared with a normal tissue of MMR-deficient mice. The elevated mutation frequencies in the lymphoid tumors, and the finding of multiple clustered mutations in lacI genes rescued from these tumors, suggest that they are possibly generated by a lymphoma-specific hypermutational mechanism.

L10 ANSWER 2 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2000149898 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10684825
TITLE: Expression of deoxyribonucleic acid repair enzymes during spermatogenesis in mice.
AUTHOR: Richardson L L; Pedigo C; Ann Handel M
CORPORATE SOURCE: Department of Biochemistry and Cellular and Molecular Biology, University of Tennessee, Knoxville, Tennessee 37996-0840, USA.. lrichar5@utk.edu
CONTRACT NUMBER: HD31376 (NICHD)
SOURCE: Biology of reproduction, (2000 Mar) 62 (3) 789-96.
Journal code: 0207224. ISSN: 0006-3363.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20020919
Entered Medline: 20000412

AB Meiotic recombination during gametogenesis is critical for proper chromosome segregation. However, the participating proteins and mechanics of recombination are not well understood in mammals. DNA repair enzymes play an essential role in both mitosis and meiosis in yeast. The mammalian **mismatch repair** system consists of homologues of the **bacterial** MutH, MutL, and MutS proteins. As

part of our goal of understanding the function of enzymes that mediate meiotic recombination, we used a reverse transcription-polymerase chain reaction approach to identify germ cell transcripts for the MutL homologue, **Pms2**, and two members of the MutS family, Msh2 and Msh3. Both the **Pms2** and the Msh2 genes were highly expressed in mitotically proliferating spermatogonia, and early in meiotic prophase in the leptotene and zygotene spermatocytes. Thereafter, expression declined in early and mid pachytene spermatocytes, and was negligible in postmeiotic spermatids. In contrast, expression of Msh3 was at its highest level in pachytene spermatocytes. Protein levels were similar to gene expression patterns, and both **PMS2** and MSH2 were localized in spermatogonia and spermatocytes. These patterns of expression for genes encoding **mismatch repair** enzymes are consistent with the proposed roles of the gene products in **mismatch repair** during both DNA replication and recombination.

L10 ANSWER 3 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2000082804 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10615123
TITLE: MLH3: a DNA mismatch repair gene associated with mammalian microsatellite instability.
AUTHOR: Lipkin S M; Wang V; Jacoby R; Banerjee-Basu S; Baxevanis A D; Lynch H T; Elliott R M; Collins F S
CORPORATE SOURCE: Genetics Branch, National Human Genome Research Institute, Bethesda, Maryland, USA.
CONTRACT NUMBER: CA62225 (NCI)
SOURCE: Nature genetics, (2000 Jan) 24 (1) 27-35.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF195657; GENBANK-AF195658; GENBANK-AL031135; GENBANK-P14242; GENBANK-P49850; GENBANK-P54277; GENBANK-P54278; GENBANK-Z73520; GENBANK-Z92813
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000210

AB DNA **mismatch repair** is important because of its role in maintaining genomic integrity and its association with hereditary non-polyposis colon cancer (HNPCC). To identify new human **mismatch repair** proteins, we probed nuclear extracts with the conserved carboxy-terminal MLH1 interaction domain. Here we describe the cloning and complete genomic sequence of MLH3, which encodes a new DNA **mismatch repair** protein that interacts with MLH1. MLH3 is more similar to **mismatch repair** proteins from yeast, plants, worms and **bacteria** than to any known mammalian protein, suggesting that its conserved sequence may confer unique functions in mice and humans. Cells in culture stably expressing a dominant-negative MLH3 protein exhibit microsatellite instability. Mlh3 is highly expressed in gastrointestinal epithelium and physically maps to the mouse complex trait locus colon cancer susceptibility I (Ccs1). Although we were unable to identify a mutation in the protein-coding region of Mlh3 in the susceptible mouse strain, colon tumours from congenic Ccs1 mice exhibit microsatellite instability. Functional redundancy among Mlh3, Pms1 and **Pms2** may explain why neither Pms1 nor **Pms2** mutant mice develop colon cancer, and why PMS1 and **PMS2** mutations are only rarely found in HNPCC families.

L10 ANSWER 4 OF 16 MEDLINE on STN
ACCESSION NUMBER: 1999203588 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10101297

TITLE: The human **PMS2L** proteins do not interact with hMLH1, a major DNA **mismatch repair** protein.
AUTHOR: Kondo E; Horii A; Fukushige S
CORPORATE SOURCE: Department of Molecular Pathology, Tohoku University School of Medicine, Sendai, Miyagi, 980-8575, Japan.
SOURCE: Journal of biochemistry, (1999 Apr) 125 (4) 818-25.
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB017004; GENBANK-AB017005; GENBANK-AB017006; GENBANK-AB017007
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 20020420
Entered Medline: 19990805

AB The human **PMS2** gene encodes one of the **bacterial** mutL homologs that is associated with hereditary nonpolyposis colorectal cancer (HNPCC). One of the interesting features of the hPMS2 gene is that it is part of a multiple gene family which is localized on chromosome bands 7p22, 7p12-p13, 7q11, and 7q22. Here we report four newly identified hPMS2-like (**PMS2L**) genes. All four novel members of the **PMS2L** gene family encode relatively short polypeptides composed of the amino-terminal portion of hPMS2 and are expressed ubiquitously except in the heart. To clarify whether the **PMS2L** polypeptides contribute to the DNA **mismatch repair** (MMR) pathway through an interaction with hMLH1, we have performed a yeast two-hybrid assay and an immunoprecipitation study using an hPMS2 mutant cell line, HEC-1-A. Our results clearly indicate that hMLH1 does not interact with two representative PMS2Ls, whereas the carboxyl-terminal portion of hPMS2, not the amino-terminal portion, does interact with hMLH1. Thus, PMS2Ls are not likely to participate in the MMR pathway through association with hMLH1; they must play some other roles in the living cells.

L10 ANSWER 5 OF 16 MEDLINE on STN
ACCESSION NUMBER: 97264596 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9110401
TITLE: DNA mismatch repair deficient mice in cancer research.
AUTHOR: Prolla T A; Abuin A; Bradley A
CORPORATE SOURCE: Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030, USA.
SOURCE: Seminars in cancer biology, (1996 Oct) 7 (5) 241-7. Ref: 67
Journal code: 9010218. ISSN: 1044-579X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970606

AB Biochemical and genetic approaches have been used to demonstrate that basic elements of a DNA **mismatch repair** (MMR) pathway are conserved between **bacteria**, yeast and mammals. Recently, mutations in the human MMR genes MSH2, MLH1, PMS1 and **PMS2** have been implicated in a common form of hereditary colon cancer and in sporadic tumors of various tissues. In order to better understand the consequences of MMR deficiency in mammalian organisms, mice deficient for

the **Pms2**, Mlh1 and Msh2 MMR gene homologues have been generated. MMR deficient mice display a general increase in spontaneous mutation rate and develop tumors during the first year of life. Additionally, loss of MMR appears to accelerate tumorigenesis in an Apc deficient background.

L10 ANSWER 6 OF 16 MEDLINE on STN
ACCESSION NUMBER: 97250500 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9096356
TITLE: Elevated levels of mutation in multiple tissues of mice deficient in the DNA **mismatch repair** gene **Pms2**.
AUTHOR: Narayanan L; Fritzell J A; Baker S M; Liskay R M; Glazer P M
CORPORATE SOURCE: Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT 06520-8040, USA.
CONTRACT NUMBER: ES05775 (NIEHS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Apr 1) 94 (7) 3122-7. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 20020420
Entered Medline: 19970508

AB The **Pms2** gene has been implicated in hereditary colon cancer and is one of several mammalian homologs of the Escherichia coli mutL DNA **mismatch repair** gene. To determine the effect of **Pms2** inactivation on genomic integrity in vivo, hybrid transgenic mice were constructed that carry targeted disruptions at the **Pms2** loci along with a chromosomally integrated mutation reporter gene. In the absence of any mutagenic treatment, mice nullizygous for **Pms2** showed a 100-fold elevation in mutation frequency in all tissues examined compared with both wild-type and heterozygous litter mates. The mutation pattern in the nullizygotes was notable for frequent 1-bp deletions and insertions within mononucleotide repeat sequences, consistent with an essential role for **PMS2** in the repair of replication slippage errors. Further, the results demonstrate that high rates of mutagenesis in multiple tissues are compatible with normal development and life and are not necessarily associated with accelerated aging. Also, the finding of genetic instability in all tissues tested contrasts with the limited tissue distribution of cancers in the animals, raising important questions regarding the role of mutagenesis in carcinogenesis.

L10 ANSWER 7 OF 16 EMBASE on STN
ACCESSION NUMBER: 2000080397 EMBASE
TITLE: Expression of deoxyribonucleic acid repair enzymes during spermatogenesis in mice.
AUTHOR: Richardson L.L.; Pedigo C.; Handel M.A.
CORPORATE SOURCE: L.L. Richardson, Department of Biochemistry, Walters Life Sciences Building, University of Tennessee, 1414 Cumberland Avenue, Knoxville, TN 37996-0840, United States. lrichar5@utk.edu
SOURCE: Biology of Reproduction, (2000) 62/3 (789-796). Refs: 42
ISSN: 0006-3363 CODEN: BIREBV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
021 Developmental Biology and Teratology

029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Meiotic recombination during gametogenesis is critical for proper chromosome segregation. However, the participating proteins and mechanics of recombination are not well understood in mammals. DNA **repair** enzymes play an essential role in both mitosis and meiosis in yeast. The mammalian **mismatch repair** system consists of homologues of the **bacterial** MutH, MutL, and MutS proteins. As part of our goal of understanding the function of enzymes that mediate meiotic recombination, we used a reverse transcription-polymerase chain reaction approach to identify germ cell transcripts for the MutL homologue, **Pms2**, and two members of the MutS family, Msh2 and Msh3. Both the **Pms2** and the Msh2 genes were highly expressed in mitotically proliferating spermatogonia, and early in meiotic prophase in the leptotene and zygotene spermatocytes. Thereafter, expression declined in early and mid pachytene spermatocytes, and was negligible in postmeiotic spermatids. In contrast, expression of Msh3 was at its highest level in pachytene spermatocytes. Protein levels were similar to gene expression patterns, and both **PMS2** and MSH2 were localized in spermatogonia and spermatocytes. These patterns of expression for genes encoding **mismatch repair** enzymes are consistent with the proposed roles of the gene products in **mismatch repair** during both DNA replication and recombination.

L10 ANSWER 8 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000028431 EMBASE
TITLE: MLH3: A DNA mismatch repair gene associated with mammalian microsatellite instability.
AUTHOR: Lipkin S.M.; Wang V.; Jacoby R.; Banerjee-Basu S.; Baxevanis A.D.; Lynch H.T.; Elliott R.M.; Collins F.S.
CORPORATE SOURCE: F.S. Collins, Genetics and Molec. Biology Branch, Genome Technology Branch, Natl. Human Genome Res. Institute, Bethesda, MD, United States
SOURCE: Nature Genetics, (2000) 24/1 (27-35).
ISSN: 1061-4036 CODEN: NGENEC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB DNA **mismatch repair** is important because of its role in maintaining genomic integrity and its association with hereditary non-polyposis colon cancer (HNPCC). To identify new human **mismatch repair** proteins, we probed nuclear extracts with the conserved carboxy-terminal MLH1 interaction domain. Here we describe the cloning and complete genomic sequence of MLH3, which encodes a new DNA **mismatch repair** protein that interacts with MLH1. MLH3 is more similar to **mismatch repair** proteins from yeast, plants, worms and **bacteria** than to any known mammalian protein, suggesting that its conserved sequence may confer unique functions in mice and humans. Cells in culture stably expressing a dominant-negative MLH3 protein exhibit microsatellite instability. Mlh3 is highly expressed in gastrointestinal epithelium and physically maps to the mouse complex trait locus colon cancer susceptibility I (Ccs1). Although we were unable to identify a mutation in the protein- coding region of Mlh3 in the susceptible mouse strain, colon tumours from congenic Ccs1 mice exhibit microsatellite instability. Functional redundancy among Mlh3, Pms1 and **Pms2** may explain why neither Pms1 nor **Pms2** mutant mice develop colon cancer, and why PMS1 and **PMS2** mutations are only rarely found in HNPCC families.

L10 ANSWER 9 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999146454 EMBASE
TITLE: The human **PMS2L** proteins do not interact with hMLH1, a major DNA **mismatch repair** protein.
AUTHOR: Kondo E.; Horii A.; Fukushige S.
CORPORATE SOURCE: S. Fukushige, Department of Molecular Pathology, Tohoku University School of Medicine, Sendai, Miyagi 980-8575, Japan. shinichi@mail.cc.tohoku.ac.jp
SOURCE: Journal of Biochemistry, (1999) 125/4 (818-825).
Refs: 15
ISSN: 0021-924X CODEN: JOBIAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The human **PMS2** gene encodes one of the **bacterial** mutL homologs that is associated with hereditary nonpolyposis colorectal cancer (HNPCC). One of the interesting features of the hPMS2 gene is that it is part of a multiple gene family which is localized on chromosome bands 7p22, 7p12-p13, 7q11, and 7q22. Here we report four newly identified hPMS2-like (**PMS2L**) genes. All four novel members of the **PMS2L** gene family encode relatively short polypeptides composed of the amino-terminal portion of hPMS2 and are expressed ubiquitously except in the heart. To clarify whether the **PMS2L** polypeptides contribute to the DNA **mismatch repair** (MMR) pathway through an interaction with hMLH1, we have performed a yeast two-hybrid assay and an immunoprecipitation study using an hPMS2 mutant cell line, HEC-1-A. Our results clearly indicate that hMLH1 does not interact with two representative PMS2Ls, whereas the carboxyl-terminal portion of hPMS2, not the amino-terminal portion, does interact with hMLH1. Thus, PMS2Ls are not likely to participate in the MMR pathway through association with hMLH1; they must play some other roles in the living cells.

L10 ANSWER 10 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 97128139 EMBASE
DOCUMENT NUMBER: 1997128139
TITLE: DNA mismatch repair deficient mice in cancer research.
AUTHOR: Prolla T.A.; Abuin A.; Bradley A.
CORPORATE SOURCE: T.A. Prolla, Department Molecular Human Genetics, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States
SOURCE: Seminars in Cancer Biology, (1996) 7/5 (241-247).
Refs: 67
ISSN: 1044-579X CODEN: SECBE7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Biochemical and genetic approaches have been used to demonstrate that basic elements of a DNA **mismatch repair** (MMR) pathway are conserved between **bacteria**, yeast and mammals. Recently, mutations in the human MMR genes MSH2, MLH1, PMS1 and **PMS2** have been implicated in a common form of hereditary colon cancer and in sporadic tumors of various tissues. In order to better understand the consequences of MMR deficiency in mammalian organisms, mice deficient for the **Pms2**, Mlh1 and Msh2 MMR gene homologues have been generated. MMR deficient mice display a general increase in spontaneous mutation rate

and develop tumors during the first year of life. Additionally, loss of MMR appears to accelerate tumorigenesis in an Apc deficient background.

L10 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:190645 BIOSIS
DOCUMENT NUMBER: PREV200000190645
TITLE: MLH3: A DNA mismatch repair gene associated with mammalian microsatellite instability.
AUTHOR(S): Lipkin, Steven M.; Wang, Victoria; Jacoby, Russell; Banerjee-Basu, Sharmila; Baxevanis, Andreas D.; Lynch, Henry T.; Elliott, Rosemary M.; Collins, Francis S. [Reprint author]
CORPORATE SOURCE: Genetics and Molecular Biology Branch, National Human Genome Research Institute, Bethesda, MD, USA
SOURCE: Nature Genetics, (Jan., 2000) Vol. 24, No. 1, pp. 27-35. print.
ISSN: 1061-4036.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 May 2000
Last Updated on STN: 4 Jan 2002

AB DNA **mismatch repair** is important because of its role in maintaining genomic integrity and its association with hereditary non-polyposis colon cancer (HNPCC). To identify new human **mismatch repair** proteins, we probed nuclear extracts with the conserved carboxy-terminal MLH1 interaction domain. Here we describe the cloning and complete genomic sequence of MLH3, which encodes a new DNA **mismatch repair** protein that interacts with MLH1. MLH3 is more similar to **mismatch repair** proteins from yeast, plants, worms and **bacteria** than to any known mammalian protein, suggesting that its conserved sequence may confer unique functions in mice and humans. Cells in culture stably expressing a dominant-negative MLH3 protein exhibit microsatellite instability. Mlh3 is highly expressed in gastrointestinal epithelium and physically maps to the mouse complex trait locus colon cancer susceptibility I (Ccs1). Although we were unable to identify a mutation in the protein-coding region of Mlh3 in the susceptible mouse strain, colon tumours from congenic Ccs1 mice exhibit microsatellite instability. Functional redundancy among Mlh3, Pms1 and **Pms2** may explain why neither Pms1 nor **Pms2** mutant mice develop colon cancer, and why PMS1 and **PMS2** mutations are only rarely found in HNPCC families.

L10 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:175455 BIOSIS
DOCUMENT NUMBER: PREV200000175455
TITLE: Expression of deoxyribonucleic acid repair enzymes during spermatogenesis in mice.
AUTHOR(S): Richardson, Laura L. [Reprint author]; Pedigo, Camille; Handel, Mary Ann
CORPORATE SOURCE: Department of Biochemistry and Cellular and Molecular Biology, University of Tennessee, 1414 Cumberland Avenue, Room M407 Walters Life Sciences Building, Knoxville, TN, 37996-0840, USA
SOURCE: Biology of Reproduction, (March, 2000) Vol. 62, No. 3, pp. 789-796. print.
CODEN: BIREBV. ISSN: 0006-3363.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 May 2000
Last Updated on STN: 4 Jan 2002

AB Meiotic recombination during gametogenesis is critical for proper chromosome segregation. However, the participating proteins and mechanics of recombination are not well understood in mammals. DNA repair enzymes

play an essential role in both mitosis and meiosis in yeast. The mammalian **mismatch repair** system consists of homologues of the **bacterial** MutH, MutL, and MutS proteins. As part of our goal of understanding the function of enzymes that mediate meiotic recombination, we used a reverse transcription-polymerase chain reaction approach to identify germ cell transcripts for the MutL homologue, **Pms2**, and two members of the MutS family, Msh2 and Msh3. Both the **Pms2** and the Msh2 genes were highly expressed in mitotically proliferating spermatogonia, and early in meiotic prophase in the leptotene and zygotene spermatocytes. Thereafter, expression declined in early and mid pachytene spermatocytes, and was negligible in postmeiotic spermatids. In contrast, expression of Msh3 was at its highest level in pachytene spermatocytes. Protein levels were similar to gene expression patterns, and both **PMS2** and MSH2 were localized in spermatogonia and spermatocytes. These patterns of expression for genes encoding **mismatch repair** enzymes are consistent with the proposed roles of the gene products in **mismatch repair** during both DNA replication and recombination.

L10 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:324863 BIOSIS
DOCUMENT NUMBER: PREV199900324863
TITLE: The human **PMS2L** proteins do not interact with hMLH1, a major DNA **mismatch repair** protein.
AUTHOR(S): Kondo, Emiko; Horii, Akira; Fukushige, Shinichi [Reprint author]
CORPORATE SOURCE: Department of Molecular Pathology, Tohoku University School of Medicine, Sendai, Miyagi, 980-8575, Japan
SOURCE: Journal of Biochemistry (Tokyo), (April, 1999) Vol. 125, No. 4, pp. 818-825. print.
CODEN: JOBIAO. ISSN: 0021-924X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

AB The human **PMS2** gene encodes one of the **bacterial** mutL homologs that is associated with hereditary nonpolyposis colorectal cancer (HNPCC). One of the interesting features of the hPMS2 gene is that it is part of a multiple gene family which is localized on chromosome bands 7p22, 7p12-p13, 7q11, and 7q22. Here we report four newly identified hPMS2-like (**PMS2L**) genes. All four novel members of the **PMS2L** gene family encode relatively short polypeptides composed of the amino-terminal portion of hPMS2 and are expressed ubiquitously except in the heart. To clarify whether the **PMS2L** polypeptides contribute to the DNA **mismatch repair** (MMR) pathway through an interaction with hMLH1, we have performed a yeast two-hybrid assay and an immunoprecipitation study using an hPMS2 mutant cell line, HEC-1-A. Our results clearly indicate that hMLH1 does not interact with two representative PMS2Ls, whereas the carboxyl-terminal portion of hPMS2, not the amino-terminal portion, does interact with hMLH1. Thus,PMS2Ls are not likely to participate in the MMR pathway through association with hMLH1; they must play some other roles in the living cells.

L10 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:377393 BIOSIS
DOCUMENT NUMBER: PREV199799676596
TITLE: Transcription-coupled repair and human disease.
AUTHOR(S): Mellon, I.; Champe, G. N.; Rajpal, D. K.; Adkins, M.
CORPORATE SOURCE: Dep. Pathol., Program Toxicol., Markey Cancer Cent., Univ. Ky., Lexington, KY 40536, USA
SOURCE: Photochemistry and Photobiology, (1997) Vol. 65, No. SPEC. ISSUE, pp. 53S.

Meeting Info.: 25th Annual Meeting of the American Society for Photobiology. St. Louis, Missouri, USA. July 5-10, 1997.
CODEN: PHCBAP. ISSN: 0031-8655.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

L10 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:319348 BIOSIS
DOCUMENT NUMBER: PREV199699041704
TITLE: Saccharomyces cerevisiae pms2 mutations are alleles of MLH1, and pms2-2 corresponds to a hereditary nonpolyposis colorectal carcinoma-causing missense mutation.
AUTHOR(S): Jeyaprakash, A.; Gupta, Ruchira Das; Kolodner, Richard [Reprint author]
CORPORATE SOURCE: Dana-Farber Cancer Inst., 44 Binney St., Boston, MA 02115, USA
SOURCE: Molecular and Cellular Biology, (1996) Vol. 16, No. 6, pp. 3008-3011.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 1996
Last Updated on STN: 11 Jul 1996

AB A number of mutant Saccharomyces cerevisiae strains having phenotypes consistent with defects in DNA **mismatch repair** have been described, but not all have been extensively characterized. In this study we demonstrated that the **pms2**-1 and **pms2**-2 alleles arise from missense mutations in the MLH1 gene which inactivate MLH1. One of these alleles, **pms2**-2, causes the same amino acid substitution in a highly conserved region of the known MutL homologs as that caused by a proposed missense mutation observed in a Swedish hereditary nonpolyposis colorectal carcinoma kindred. This observation supports the functional significance of missense mutations found in hereditary nonpolyposis colorectal carcinoma kindreds and indicates that in some cases S. cerevisiae can serve as a useful model system for the analysis of such mutations.

L10 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1989:514164 BIOSIS
DOCUMENT NUMBER: PREV198988130307; BA88:130307
TITLE: HETERODUPLEX DNA CORRECTION IN SACCHAROMYCES-CEREVISIAE IS MISMATCH SPECIFIC AND REQUIRES FUNCTIONAL PMS GENES.
AUTHOR(S): KRAMER B [Reprint author]; KRAMER W; WILLIAMSON M S; FOGEL S
CORPORATE SOURCE: INST FUER MOL GENETIK DER GEORG-AUGUST-UNIV GOETTINGEN, GRISEBACHSTRASSE 8, D-3400 GOETTINGEN, FRG
SOURCE: Molecular and Cellular Biology, (1989) Vol. 9, No. 10, pp. 4432-4440.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 15 Nov 1989
Last Updated on STN: 15 Nov 1989

AB In vitro-constructed heteroduplex DNAs with defined mismatches were corrected in Saccharomyces cerevisiae cells with efficiencies that were dependent on the mismatch. Single-nucleotide loops were repaired very efficiently; the base/base mismatches G/T, A/C, G/G, A/G, G/A, A/A, T/T, T/C, and C/T were repaired with a high a intermediate efficiency. The

mismatch C/C and a 38-nucleotide loop were corrected with low efficiency. This substrate specificity pattern resembles that found in Escherichia coli and Streptococcus pneumoniae, suggesting an evolutionary relationship of DNA **mismatch repair** in pro- and eucaryotes.
Repair of the listed mismatches was severely impaired in the putative S. cerevisiae DNA **mismatch repair** mutants pms1 and **pms2**. Low-efficiency repair also characterized pms3 strains, except that correction of single-nucleotide loops occurred with an efficiency close to that of PMS wild-type strains. A close correlation was found between the repair efficiencies determined in this study and the observed postmeiotic segregation frequencies of alleles with known DNA sequence. This suggests an involvement of DNA **mismatch repair** in recombination and gene conversion in S. cerevisiae.